

T CELL RECEPTORS THAT RECOGNIZE THE TYROSINASE TUMOR ANTIGEN

SUMMARY

The National Cancer Institute, Surgery Branch, Tumor Immunology Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize T Cells Attacking Cancer: T Cell Receptors that Recognize the Tyrosinase Tumor Antigen

REFERENCE NUMBER

E-043-2009

PRODUCT TYPE

- Therapeutics

KEYWORDS

- Adoptive Cell Transfer
- Immunotherapy
- T cell receptors (TCRs)
- tyrosinase tumor-associated antigen (TAA)

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

The [National Cancer Institute's Tumor Immunology Section](#) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize new approaches to the immunotherapy of patients with cancer.

There is an urgent need to develop new therapeutic strategies combining fewer side-effects and more specific anti-tumor activity. Adoptive cell transfer (ACT) is a promising new immunotherapeutic approach to treat cancer and other diseases by directing an individual's innate and adaptive immune system to recognize specific disease-associated antigens.

T cell receptors (TCRs) are proteins that recognize antigens in the context of infected or transformed cells and activate T cells to mediate an immune response and destroy abnormal cells. TCRs consist of two

domains, one variable domain that recognizes the antigen and one constant region that helps the TCR anchor to the membrane and transmit recognition signals by interacting with other proteins.

Scientists at the National Cancer Institute (NCI) have isolated T cells that recognize the human tyrosinase tumor-associated antigen (TAA) from the tumor infiltrating lymphocytes (TIL) of a melanoma cancer patient. The human tyrosinase antigen is a tumor antigen expressed in a variety of cancers, including skin cancer (melanoma) and brain cancer (glioblastoma). Utilizing the tyrosinase specific T cells, these scientists developed human/mouse hybrid TCRs with enhanced affinity for the tyrosinase TAA and that can be expressed in both CD8 and CD4 T cells. T cells expressing these engineered TCRs recognize skin and brain tumor cells in culture. These T cells also exhibit enhanced cytokine induction and better tumor reactivity compared to unmodified TCRs.

Previous versions of gene-modified T cells developed by NIH researchers demonstrated objective clinical responses in some cancer patients, which have validated gene-modified T cell immunotherapy as a promising cancer treatment strategy. TCRs directed against the tyrosinase TAA could serve as valuable new immunotherapeutic tools for attacking tumors, especially in patients whose tumors do not express other common TAAs.

This technology is in the pre-clinical stage of development. The inventors plan to develop the technology into clinical grade reagent for a clinical trial if the pre-clinical data continues to show promising results.

Further R&D Needed:

- Continued testing of engineered cells for reactivity against tumor cell lines and fresh tumor samples.
- Development into clinical grade reagent for TCR gene therapy trials at NCI

POTENTIAL COMMERCIAL APPLICATIONS

- Immunotherapeutics to treat and/or prevent the reoccurrence of a variety of human cancers, including melanomas and glioblastomas
- A drug component of a combination immunotherapy regimen aimed at targeting the specific tumor-associated antigens expressed by the cancer cells of individual patients.

COMPETITIVE ADVANTAGES

- The parent tyrosinase-specific TCR was isolated from tumor infiltrating lymphocytes, so the genetically-modified versions should have an elevated affinity for tyrosinase.
- The tyrosinase-specific T cells recognize skin and brain cancer cells in culture. These T cells are predicted to have broad anti-cancer activity once developed to a clinical level.
- CD8 independency: The tyrosinase-specific TCRs can be expressed in both CD8 and CD4 T cells to maximize the cell-mediated immune response to the tumor.
- The tyrosinase-specific T cells should not be rejected by a patient's immune system since the mouse TCR sequences are incorporated into a human TCR backbone.

INVENTOR(S)

- [Steven A Rosenberg](#) (NCI)

DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PATENT STATUS

- **U.S. Filed:** U.S. Provisional Application No. 61/005,363 filed 03 Dec 2007

THERAPEUTIC AREA

- Cancer/Neoplasm